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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,668	01/06/2006	Stephen Robert Wedge	056291-5229	1521

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EXAMINER	
RAO, SAVITHA M	

ART UNIT	PAPER NUMBER
4131	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,668	WEDGE ET AL.	
	Examiner	Art Unit	
	SAVITHA RAO	4131	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/06/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claim:

Claims 1-13 are pending and are subject of this office action.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statement filed 01/06/2006. The Examiner has considered the reference cited therein to the extent that each is a proper citation. Please see the attached USPTO Form 1449.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 12-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention

The term "reducing effect" in claims 1, 4, 7-9, 12-13 is a relative term which renders the claim indefinite. The term "reducing effect" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Regarding claims 1-6 and 12-13 the phrase "such as" renders the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 1-9 provides for the "use of ZD6474 and a platinum anti tumor agent in the manufacture of a medicament for use in the production of an anti-angiogenic and/or vascular permeability reducing effect or anti-cancer or anti-tumor effect in warm-blooded animal such as a human", but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-9 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious

at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co,, 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:
1. Determining the scope and contents of the prior art. 2. Ascertaining the differences between the prior art and the claims at issue. 3. Resolving the level of ordinary skill in the pertinent art. 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Use claims 1-9 of the instant application are being considered as method claims in the instant office action.

Instant claims 1-6, 10-13 are rejected under 35 U.S.C 103 (a) as being unpatentable over Hannequin et. al (WO 01/32651, IDS reference) in view of Kuenen et al (Journal of Clinical Oncology, Vol 20, pp 1657-1667 (March 2002) and Gorski et al (Cancer Research, Vol 59, pp. 3374-3378 (jul 1999), IDS reference).

Claims 1-6 are drawn to a use of ZD6474 combined with platinum anti-tumor agent in the manufacture of a medicament for use in the production of anti-angiogenic or anti-cancer or anti-tumor effect in a warm blooded animal such as human, optionally in addition to treatment with ionizing radiation. Claim 10 and 11 are drawn to a pharmaceutical composition and a kit respectively comprising ZD6474 and a platinum anti-tumor agent. Claims 12-13 is drawn to a method for the production of an anti-angiogenic and/or vascular permeability reducing effect in a warm-blooded animal such as a human comprising administering an effective amount of ZD6474, platinum anti-tumor agent with an effective amount of ionizing radiation.

Hennequin et al discloses the use of ZD6474 specifically identified as a compound of formula 1(claim 8) and teaches the use of this compound or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for use in the production of an anti-angiogenic and/or vascular permeability reducing effect in a warm-blooded animal such as a human (p.26, lines 6-10; claim 12-13).

Hannequin further teaches that the treatment could be a sole therapy or may involve, in addition to a compound of the invention one or more other substance and/or treatments used simultaneously, sequentially or by separate administration of the individual components of the treatment (p 26, lines 22-31) and suggests the use of radiotherapy (p 26, line 30) and platinum derivatives (for example cisplatin, carboplatin) in combination with ZD6474 as conjoint treatment in the field of oncology (p 27, lines 24-25)

Hannequin does not however teach the specific use of ZD6474 with platinum derivatives. This deficiency is cured by teachings of Kuenen et al. who teaches the use of cisplatin and SU5416 in patients with solid tumors. SU5416 is also a small molecule VEGF receptor inhibitor similar in its mechanism of action to ZD6474. Kuenen additionally teaches the advantages of combining angiogenesis inhibitor with chemotherapy (page 1658, paragraph 2).
Hannequin does not teach the use of ZD6474 with ionizing treatment. This deficiency is cured by Gorki et al who teaches that VEGF inhibitors, a class of compounds of which ZD6474 is a member, administered with ionizing radiation results in greater than additive anti-tumor effects (page 3378, paragraph1) Therefore it would have been obvious to one of ordinary skill in the art at the time of the instantly claimed invention to prepare a medicament using ZD6474 with concurrent radiotherapy and platinum derivatives (a well known anti-cancer drugs) to use in the treatment of cancer and in the production of an anti-angiogenic and/or vascular permeability reducing effect in a warm-blooded animal, thus resulting in the practice of the instantly claimed invention (Claims 1-6, 10-13) with a reasonable expectation of success.

Furthermore, combining ZD6474 with platinum anti-tumor agent into a pharmaceutical composition or kit (instant claims 10-11) would have been obvious to one of ordinary skill in the art at the time of invention, since they are both know chemotherapeutic agents. Applicant is reminded of *In re Kerkhoven*, which affirmed that "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to

form a third composition to be used for the very same purpose....the idea of combining them flows logically from their having been individually taught in the prior art". *In re Kerkhoven*, 626 F .2d 846, 850, 205, USPQ 1069, 1072 (CCPA 1980). The addition of a pharmaceutically acceptable carrier or excipient to the aforementioned pharmaceutical composition would have been obvious to one of ordinary skill in the art at the time of the invention and they would be motivated to do so to allow for effective administration to the patient and delivery to the targeted tissue.

One of ordinary skill in the art would have been motivated to do the above in order to develop a more powerful cancer treatment method than existing ones. One of ordinary skill in the art would have a reasonable expectation of success since each of the components has been shown to have their own anti-tumor activity. Therefore the above references in combination render claims 1-6 and 10-13 prima facia obvious to one of ordinary skill in the art.

Claims 7-9 are rejected under 35 U.S.C 103 (a) as being unpatentable over Hannequin et. al (WO 01/32651) in view of Desoize et al. (Critical reviews in Oncology/Hematology, vol 42, pp 317-325 (2002)) and Gorski et al (Cancer Research, Vol 59, pp. 3374-3378 (Jul 1999)).
Claims 7-9 are drawn to a use of ZD6474 combined with platinum anti-tumor agent wherein the platinum anti-tumor agent is Cisplatin (claim 7), Carboplatin (claim 8) and Oxoliplatin (claim 9)

Teachings of Hennequin et al has been set forth in the previous rejection above in the instant office action.

Hannequin fails to teach the use of Oxaliplatin with ZD6474. This deficiency is cured by teachings of Desoize et al. who teaches that the mechanism of action of cisplatin, carboplatin and oxalaplatin are similar in that they all are pro-drugs which form adducts with DNA, impairing DNA synthesis and repair (Abstract, Page 317), page 318-319 Chemistry and Mechanism of action section). 3378, paragraph1).

Therefore it would have been obvious to one of ordinary skill in the art at the time of the instantly claimed invention to prepare a medicament using ZD6474 with any of the claimed platinum anti-cancer agents, cisplatin or carboplatin or oxaliplatin thus resulting in the practice of the instantly claimed invention (Claims 7-9) with a reasonable expectation or success. One of ordinary skill in the art would be motivated to do so to obtain the best anti-cancer and anti-angiogenic effect from the prepared medicament. Therefore the above references in combination render claims 7-9 prima facia obvious to one of ordinary skill in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 8 am to 5 pm. if attempts to reach the examiner by telephone are unsuccessful, the

examiner's supervisors, Janet Andres can be reached on 571-272-0867 and Cecilia Tsang can be reached at 571-272-0567. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SAVITHA RAO
Examiner
Art Unit 4131

/Cecilia Tsang/

Supervisory Patent Examiner, Art Unit 4131